

REMARKS

I. Status of the Claims and Restriction

Claims 1-39 are pending in the application and claims 2, 6, 16-21, 24-29 and 31-39 stand withdrawn pursuant to the restriction requirement and election of species. Thus, claims 1, 3-5, 7-15, 22 23 and 30 are under examination and stand rejected under 35 U.S.C. §112, second paragraph, 35 U.S.C. §102 and 35 U.S.C. §103. The specific grounds for rejection, and applicant's response thereto, are set out in detail below.

II. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1, 3-5, 7-15, 22, 23 and 30 stand rejected under the second paragraph of §112 as indefinite. It is alleged that there is an omission in the steps, specifically, "a step indicating the formation of a 'peptide-peptide interaction' and an identification step" Applicants traverse.

First, applicants note that the final clause of claim 1 recites "whereby binding of said complex to said operator region identifies said LEP as a binding partner for said target peptide." This fully satisfies the preamble of the claim. Second, with respect to a peptide-peptide interaction, this is not a "step" in the sense that applicant has not control over whether this occurs or does not occur. No affirmative action on the part of applicant *causes* this to happen. It either does or does not occur depending on the ability of the target peptide and the library encoded peptide to interact. Thus, the assay may be performed with a negative result, *i.e.*, no resulting interactions. As such, it is unnecessary to include an affirmative step of causing a peptide-peptide interaction to occur.

In light of the preceding comments, applicant respectfully requests reconsideration and withdrawal of the rejection.

III. Rejections Under 35 U.S.C. §102

A. *Zhang (1999) and Zhang (2000)*

Claims 1, 3-5, 7-15, 22, 23 and 30 stand rejected as anticipated by Zhang *et al.* (2000), and claims 1, 3-5 and 7-15 stand rejected as anticipated by Zhang *et al.* (1999). As discussed in the attached Declaration of Thomas Kodadek under 37 C.F.R. §1.132, the work described in Zhang *et al.* (1999) and (2000) is not “by another” and, therefore, is not properly citable as §102(a) prior art. Thus, applicant respectfully requests reconsideration and withdrawal of the rejections.

B. *Jappelli*

Claims 1, 3-5, 8-11, 22 and 23 stand rejected as anticipated by Jappelli *et al.* Applicant traverses.

Jappelli *et al.* use a two-hybrid-like system to screen a peptide library for molecules that bind to an intact protein. This technique is indeed the same one used by the inventor to screen peptide libraries for molecules that bind linear peptide epitopes. In fact, there are numerous papers that use various techniques to screen peptide-libraries for peptides that bind a specific protein target. However, all of these use *folded, intact proteins or protein domains* as the target for the library screen. In such studies, one cannot require that the library-derived peptide (or any other molecule if a different kind of library is screened) bind at a specific position on the target.

In the present application, a far more difficult goal is sought and achieved – binding of a peptide to a discrete region on a target molecule. Short (14-15 residues) linear target peptides were employed representing a linear epitope from the target protein. In other words, the specific

target sequence was taken out of the context of the target protein and screened against a library of peptides. Thus, any hits obtained should be targeted specifically to region of the target protein represented by the target peptide. This approach is quite different from screening against an intact protein or protein domain, where one has no control over where the library-derived molecule will bind on the target surface. In the case of intact protein targets, the binding molecules derived invariably recognize pockets on the surface of the protein that are usually functionally important regions, such as sites of protein-protein interactions (see left side of FIG. 1). One never sees binding to surface loops of an intact protein target (depicted on the right side of FIG. 1).

In order to make this distinction more clear, the present claims have been amended to recite that the target peptide is 8 to 15 residues in length. Support for this amendment can be found at page 13 of the specification, lines 5-6.

In light of the preceding, applicant respectfully requests reconsideration and withdrawal of the rejection.

IV. Rejections Under 35 U.S.C. §103

Claims 1, 3-5, 8-11, 22, 23 and 30 stand rejected as obvious over Jappelli in view of U.S. Patent 6,214,561, claims 1, 3-5, 7-11, 22 and 23 stand rejected as obvious over Jappelli in view of U.S. Patent 6,610,495, and claims 1, 3-5, 8-15, 22 and 23 stand rejected as obvious over Jappelli. Applicant traverses.

As discussed above, the facial similarities of Jappelli notwithstanding, that reference teaches the use of a two-hybrid-like system to screen a peptide library for molecules that bind to *an intact protein*. As presented for reconsideration, the instant claims use *a linear peptide*

derived from a target protein. This clearly is distinct from the Jappelli reference, and thus the rejection over Jappelli alone clearly cannot stand in view of the claims as presented for reconsideration.

Moreover, though the '495 patent discusses using peptides to interrupt biological interactions, it does not describe the use of small linear peptides selected from target proteins as binding *partners* in a system such as that described by Jappelli. The '561 patent is even less relevant, cited by the examiner as only providing β -galactosidase in the context of expression assays. Thus, these references fail to provide the missing elements of the present claims.

In summary, Jappelli *et al.* is only relevant to the present invention on the grounds that the screening technique used was similar to that employed by the inventor here. But unlike Jappelli, or either of the secondary references, the present invention utilizes small, linear epitopes as binding partners in assays for identifying binding partners to discrete regions of target molecules. Not only had this not been done previously, there was widespread doubt as to whether such could be achieved prior to the work of the inventor. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

V. **Conclusion**

In light of the foregoing, applicant respectfully submits that all claims are in condition for allowance, and an early notification to that effect. Should the examiner have any questions regarding this response, a telephone call to the undersigned is invited.

Respectfully submitted,



Steven L. Highlander
Reg. No. 37,642
Attorney for Applicant

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 536-3184

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